Paper No. 40

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JACK D. KEENE,
DANIEL J. KENAN, and
DONALD E. TSAI

Appeal No. 2000-2269
Application No. 08/862,337

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2, 5, 6, 8-11, 13, 14, 21, 26-34, 49, 50, 58, 59, 68-72, 78, and 79, all of the claims remaining. Claims 1 and 26 are representative and read as follows:

1. A method of generating a nucleic acid species which is immunologically cross-reactive with an immunogen, which immunogen is not a nucleic acid, said method comprising:

combining an antigen binding protein which binds said immunogen with a degenerate pool of nucleic acid species; and then

recovering a nucleic acid species bound by said antigen binding protein from said degenerated pool, with said nucleic acid and said immunogen binding to the same antigen recognition site on said antibody.

26. An isolated nucleic acid which inhibits complex formation between an antigen binding protein and an immunogen, which immunogen is not a nucleic acid, with said nucleic acid and said immunogen binding to the same antigen recognition site on said antibody.

The examiner relies on the following references:

Gold et al. (Gold ' 163)	5,270,163	Dec. 14, 1993
Gold et al. (Gold PCT)	WO 91/19813	Dec. 26, 1991

Bock et al. (Bock), "Selection of single-stranded DNA molecules that bind and inhibit human thrombin," Nature, Vol. 355, pp. 564-566(1992)

All of the claims stand rejected under 35 U.S.C. § 103 as obvious over either of Gold '163 or Gold PCT.

All of the claims also stand rejected under 35 U.S.C. § 103 as obvious over either of Gold '163 or Gold PCT, combined with Bock.

We reverse.

Background

Appellants' specification discloses a method of making nucleic acid mimetics of non-nucleic acid antigens, i.e., nucleic acids that are specifically bound by an antibody that also binds a non-nucleic acid antigen. The specification describes the process as follows:

> [S]uitable antigen binding proteins [e.g., antibodies] are . . . combined with a degenerate pool of nucleic acid species. . . . The pool may be formed of DNA molecules or RNA molecules, with pools of RNA molecules currently preferred. . . . Each nucleic acid species in the pool includes a degenerate segment of nucleotides . . . in which each degenerate nucleotide position is randomly assigned. . . .
>
> Combining the anti-peptide antigen binding protein with the degenerate pool may be facilitated by immobilizing the antigen binding protein on a solid support and contacting the degenerate pool . . . to the solid support. . . .
>
> Typically, . . . the step of combining the degenerate pool with the antigen binding protein is followed by the step of separating nucleic acid species bound to said solid support (e.g., by washing away any unbound nucleic acid species, then eluting nucleic acid species bound to the solid support); then producing a pool of complementary nucleic acids from said nucleic acid species separated from said solid support (e.g., reverse transcribing a pool of cDNAs from a DNA or RNA pool), then amplifying the pool of complementary nucleic acids to produce a subset degenerate pool of nucleic acid species. . . . This sequence of steps may be cyclically repeated to produce numerous subset degenerate pools.

Specification, pages 10-12.

Discussion

According to Appellants, the claims stand or fall in two groups: product claims 26-34 stand or fall together and the remaining claims (directed to methods) stand or fall together. Appeal Brief, page 5. Therefore, we will limit our consideration to claims 1 and 26. Claim 1 is directed to the disclosed process of producing nucleic acid mimetics for non-nucleic acid immunogens; i.e., a process of producing a nucleic acid that is “immunologically cross-reactive with an immunogen,” by combining an antigen-binding protein with a degenerate pool of nucleic acids, and recovering a nucleic acid that binds the antigen-binding protein

at the same antigen-recognition site bound by the immunogen. Claim 26 is directed to a nucleic acid that binds an antigen binding protein at the same antigen recognition site as a non-nucleic acid immunogen; i.e., a nucleic acid produced in a process such as that of claim 1.

1. The rejection over Gold

The examiner rejected the claims as obvious in view of the teachings of either Gold '163 or Gold PCT.[1] The examiner characterized Gold as teaching

> a method for identifying nucleic acid species which interact with targets comprising the steps: a) combining a broad class of molecules including proteins, such as antigen binding proteins or antibodies, [and] receptors, such as T cell receptors . . . , with a degenerate pool of nucleic acids . . . , b) recovering a nucleic acid bound to the target at a specific site . . . , c) amplifying selected nucleic acids by cDNA synthesis followed by PCR and RNA transcription. . . . Gold also teaches the interaction of selected nucleic acids with proteins not known to bind nucleic acids . . . as well as the use of solid supports.

Examiner's Answer, page 4.

The examiner concluded that

> [i]t would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to utilize the method of Gold for the identification of targets of any molecule and any epitope. The method of Gold is not limited to the specific examples cited in the patent, and an ordinary practitioner would have been able to utilize the method of Gold to identify nucleic acids which interact with any specific desired antibody, and for the selection of nucleic acids which can compete for binding at an antibody target site.

Examiner's Answer, page 5.

[1] Although the rejection is putatively based on either Gold reference, the examiner cited only to Gold '163 when explaining the basis of the rejection. The disclosures of both Gold references appear to be identical. Therefore, we will limit our discussion to Gold '163.

Appellants argue that the nucleic acids of the present claims are different from the "nucleic acid antibodies" disclosed by Gold, in that Gold's nucleic acids are defined as capable of binding "any compound of interest," including carbohydrates, viruses, dyes, or cofactors, whereas the nucleic acids of the present claims bind only to the antigen recognition site of an antibody. Appeal Brief, page 4. Appellants argue that Gold would not have suggested the instantly claimed products and methods because "the only place in [Gold's] lengthy disclosure where a true antibody is mentioned as a target molecule is within the 'laundry list' of putative target molecules set forth at column 13, lines 54-60." Id., page 5. Appellants conclude that

> [t]his inclusion, in the Gold patent, of "antibodies" in a broad list of putative target molecules does not establish that nucleic acids binding specifically to antigen binding sites of antibodies were contemplated by Gold, or that one skilled in the art would have had a reasonable expectation of producing such nucleic acid ligands.

Id. Additionally, Appellants submitted rebuttal evidence in the form of a declaration under 37 CFR § 1.132 by inventors Jack D. Keene and Daniel J. Kenan.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). "[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." In re Fritch,

972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992). "Although couched in terms of combining teachings found in the prior art, the same inquiry must be carried out in the context of a purported obvious 'modification' of the prior art. The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." Id. at 1266, 23 USPQ2d at 1783 (citations omitted).

We agree with Appellants that the examiner has not carried his burden of showing that the claims are prima facie obvious over the prior art. We note initially that the basis of the examiner's rejection is somewhat difficult to discern, because he did not address the particular limitations of any specific claim. For example, the examiner noted that Gold differs from the claimed invention in that

> Gold does not explicitly teach the collection of antibodies from individuals, with whatever malady, for use in the assay. Gold also does not explicitly teach specific Kd values, all possible specific buffer conditions, or selection of nucleic acids which can compete for binding with an antigen at an antibody target site.

Examiner's Answer, pages 4-5. None of these limitations, however, appears in independent claims 1 or 26.

With respect to claims 1 and 26, the examiner has not identified any specific difference between what is claimed and what is disclosed in the prior art, nor has he provided any reasoning as to why the difference(s) would have been obvious to those skilled in the art. Thus, on this record, we cannot say that the examiner has carried his burden of showing that a person skilled in the art would

have found it obvious to modify the method taught by Gold in such a way as to meet the limitations of claim 1, nor has he established that Gold would have rendered obvious the product of claim 26.

The examiner's statement that "[i]t would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to utilize the method of Gold for the identification of targets of any molecule and any epitope," Examiner's Answer, page 5, is not sufficient. Claim 1 is not directed to identifying the "targets of any molecule and any epitope;" it is limited to identifying nucleic acids that bind to the antigen-recognition site of an antigen-binding protein. Likewise, claim 26 is limited to a nucleic acid that binds to the antigen-recognition site of an antigen-binding protein. The examiner has pointed to nothing in the reference that would have led those skilled in the art to the specific, claimed method or product. We conclude that the examiner has met his burden of showing that the prior art would have motivated those skilled in the art to modify Gold in such a way as to meet the limitations of the appealed claims.

Since we conclude that the examiner has not made out a prima facie case, we need not address Appellants' rebuttal evidence, presented in the Keene and Kenan declaration. We note, however, that the examiner seemed to be trying mainly to minimize the declaration's evidentiary weight, rather than to evaluate it objectively. If so, the examiner erred. "When prima facie obviousness is established and evidence is submitted in rebuttal, the decision-maker must start over. . . . The appealed claims must be reconsidered in the light of all the

evidence, and the resultant finding, that the claimed invention would or would not have been obvious, is to be made in such light. . . . [A] final finding of obviousness may of course be reached, but such finding will rest upon evaluation of all facts in evidence, uninfluenced by any earlier conclusion reached . . . upon a different record." In re Rinehart, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976).

2. The rejection over Gold and Bock

In addition to rejecting all of the claims over the Gold references, the examiner also rejected all of the claims as obvious over either Gold references combined with Bock. Again, the examiner's rejection fails to address the particular limitations of any specific claim, but Bock is purportedly cited "[w]ith regard to Kd values and to identification of inhibitors." Examiner's Answer, page 5. The examiner characterizes Bock as "teach[ing] that selection techniques can [be] applied using nucleic acids and identifying aptamers with affinities of 25-200 nM (abstract). Bock also teaches that these selected nucleic acid aptamers can inhibit enzyme function . . . by binding a specific site on the protein." Id., pages 5-6. The examiner concludes that "[i]t would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to utilize the method of Gold to identify aptamers as suggested by Bock since Bock states 'The chemical nature, size and mode of isolation of aptamers may sometimes offer advantages over existing antibody technology.'" Id., page 6.

We reverse this rejection as well. The rejection over Gold and Bock suffers from the same deficiencies as the rejection over Gold alone. The examiner has pointed to nothing in the cited references that would have led one of skill in the art to a method or product meeting the limitations of claims 1 or 26. The examiner has not, for example, identified a difference between the teachings of a specific prior art reference and a specific claim, then explained how the combination of references would nonetheless have suggested the claimed subject matter to a person skilled in the art. On this record, we cannot say that the examiner has carried his burden of showing that the claims would have been prima facie obvious.

Other Issues

Claims 1 and 26 both end with a reference to "said antibody." In both cases, "said antibody" appears to lack antecedent basis; the rest of each claim refers to an "antigen binding protein." In addition, claims 2 and 29 state that the "antigen binding protein" can be either an antibody or a T cell receptor. The examiner and Appellants may wish to consider whether claims 1 and 26 should be amended.

In addition, we note that claims 26-34 are directed to nucleic acids defined largely by their functional, rather than structural, properties. The Federal Circuit has recently clarified the application of the written description requirement of 35 U.S.C. § 112, first paragraph, to nucleic acids. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997).

The court has held that a functional definition of DNA does not satisfy the written description requirement. See Lilly, 119 F.3d at 1566, 43 USPQ2d at 1404 ("An adequate written description of a DNA . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention. Accordingly, 'an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself.'"). See also id. at 1568, 43 USPQ2d at 1406 ("A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is."). The court recently affirmed this interpretation of the written description requirement. See Enzo Biochem, Inc. v. Gen-Probe Inc., 285 F.3d 1013, 1022, 62 USPQ2d 1289, 1297 (Fed. Cir. 2002).

Upon return of this case, the examiner may wish to consider whether, under the reasoning of Lilly and Enzo, claims 26-34 should be rejected for failing to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

Summary

The examiner has not shown that the Gold references, alone or in combination with Bock, would have rendered the instant claims prima facie obvious. Therefore, the rejections under 35 U.S.C. § 103 are reversed.

REVERSED

WILLIAM F. SMITH Administrative Patent Judge	))))) BOARD OF PATENT
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